Evaluation and Diagnosis of Hypertrophic cardiomyopathy

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Nebraska Medicine

Objectives

- Define hypertrophic cardiomyopathy (HCM).
- Identify the strengths and weaknesses of different imaging modalities as it relates to HCM.
- Become well versed at identifying obstruction by spectral Doppler.
- Review HCM phenocopies that would change management strategies.

GUIDELINES AND STANDARDS

Recommendations for Multimodality Cardiovascular Imaging of Patients with Hypertrophic Cardiomyopathy: An Update from the American Society of Echocardiography, in Collaboration with the American Society of Nuclear Cardiology, the Society for Cardiovascular Magnetic Resonance, and the Society of Cardiovascular Computed Tomography

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Definition-Adults

- Wall thickness greater than or equal to 15mm, in the absence of other causal cardiac, systemic, syndromic or metabolic disease.
  - In otherwords, "hypertrophy unexplained by loading conditions".
  - OR >12 and FH of HCM of known disease-causing genetic mutation.

- Hypertrophy is usually asymmetric, affecting non-contiguous LV segments, occasionally the RV.
  - Variants include basal septum (most common), sigmoid septum, reverse curvature, concentric, and apical.

- Largely attributed to genetic mutation in sarcomere proteins.

Multimodality approach

- H&P and ECG

- Echo
- CMR
- Cardiac CT
- Nuclear imaging

ESC European Society of Cardiology
European Heart Journal (2018) **39**, 1466–1480
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CURRENT OPINION
Coronary artery disease

International recommendations for electrocardiographic interpretation in athletes

Sanjay Sharma[1]*†, Jonathan A. Drezner[2†], Aaron Baggish[3], Michael Papadakis[1], Mathew G. Wilson[4], Jordan M. Prutkin[5], Andre La Gerche[6], Michael J. Ackerman[7], Mats Borjesson[8], Jack C. Salerno[9], Irfan M. Asif[10], David S. Owens[5], Eugene H. Chung[11], Michael S. Emery[12], Victor F. Froelicher[13], Hein Heidbuchel[14,15], Carmen Adamuz[4], Chad A. Asplund[16], Gordon Cohen[17], Kimberly G. Harmon[2], Joseph C. Marek[18], Silvana Molossi[19], Josef Niebauer[20], Hank F. Pelto[2], Marco V. Perez[21], Nathan R. Riding[4], Tess Saarel[22], Christian M. Schmied[23], David M. Shipon[24], Ricardo Stein[25], Victoria L. Vetter[26], Antonio Pelliccia[27], and Domenico Corrado[28]

Echocardiography

- Initial imaging modality of choice.
- Critical to avoid apical foreshortening in order not to miss ApHCM or apical aneurysms, crypts.
- Low threshold to utilize contrast to identify/measure all segments.
  - Would also have the benefit of myocardial target localization for alcohol septal ablation.
- Avoid pitfalls of measuring RV trabeculations, moderator band, and crista supraventricularis.

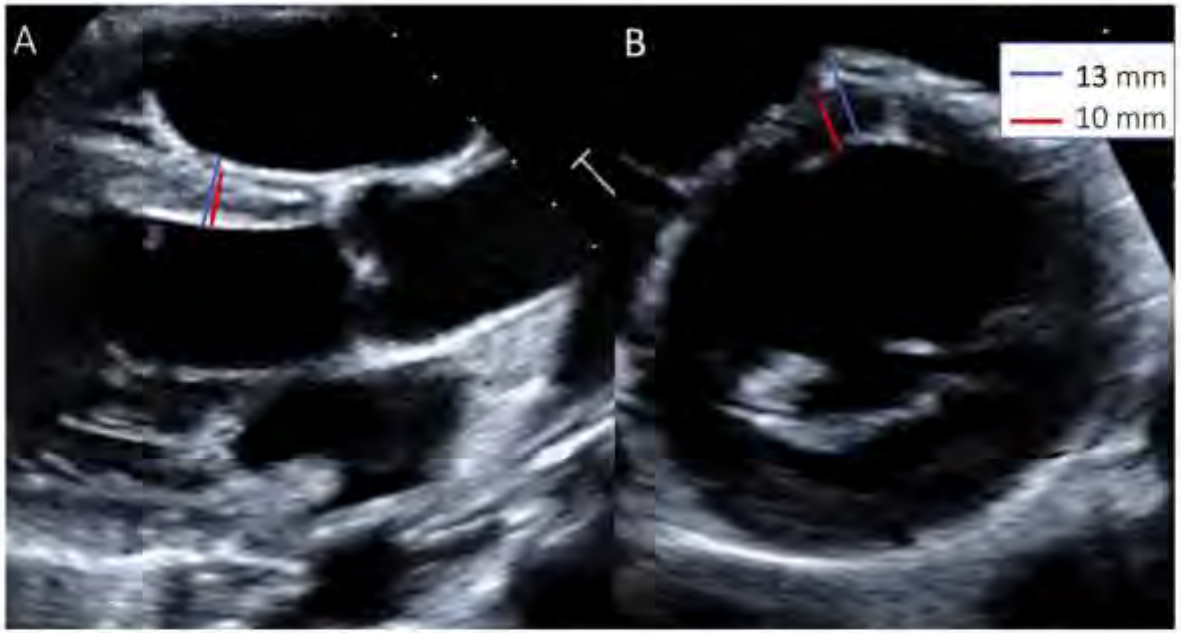


Figure 2 Challenges in measuring septal wall thickness with echocardiography. Female endurance athlete referred for evaluation of possible hypertrophic cardiomyopathy based on interventricular septal wall (IVS) measurement of 13 mm. Panels A and B are representative parasternal long-axis (PLAX) and short-axis (PSAX) images, respectively, which demonstrate inaccurate IVS measurement (*blue line*) that included right ventricular (RV) trabeculation. Comparison of the PLAX and PSAX views can help differentiate the true contractile IVS (*red line*) from RV trabeculation.

Pitfalls

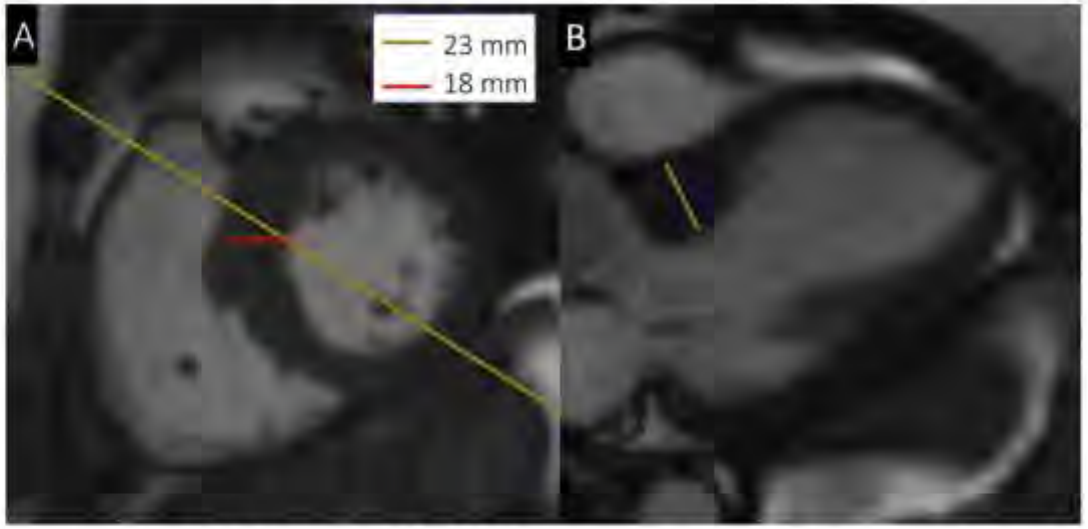


Figure 3 Challenges in measuring wall thickness with CMR. Cardiac magnetic resonance imaging demonstrating how tangential cuts through septum can overestimate interventricular septal (IVS) thickness on long-axis views. In the short-axis view **(A)**, the *yellow line* represents the plane used to obtain the long-axis view **(B)**. This line clearly cuts the muscle tangentially, which will overestimate the septal thickness, while the *red line* represents a more accurate nontangential plane through the compacted IVS thickness.

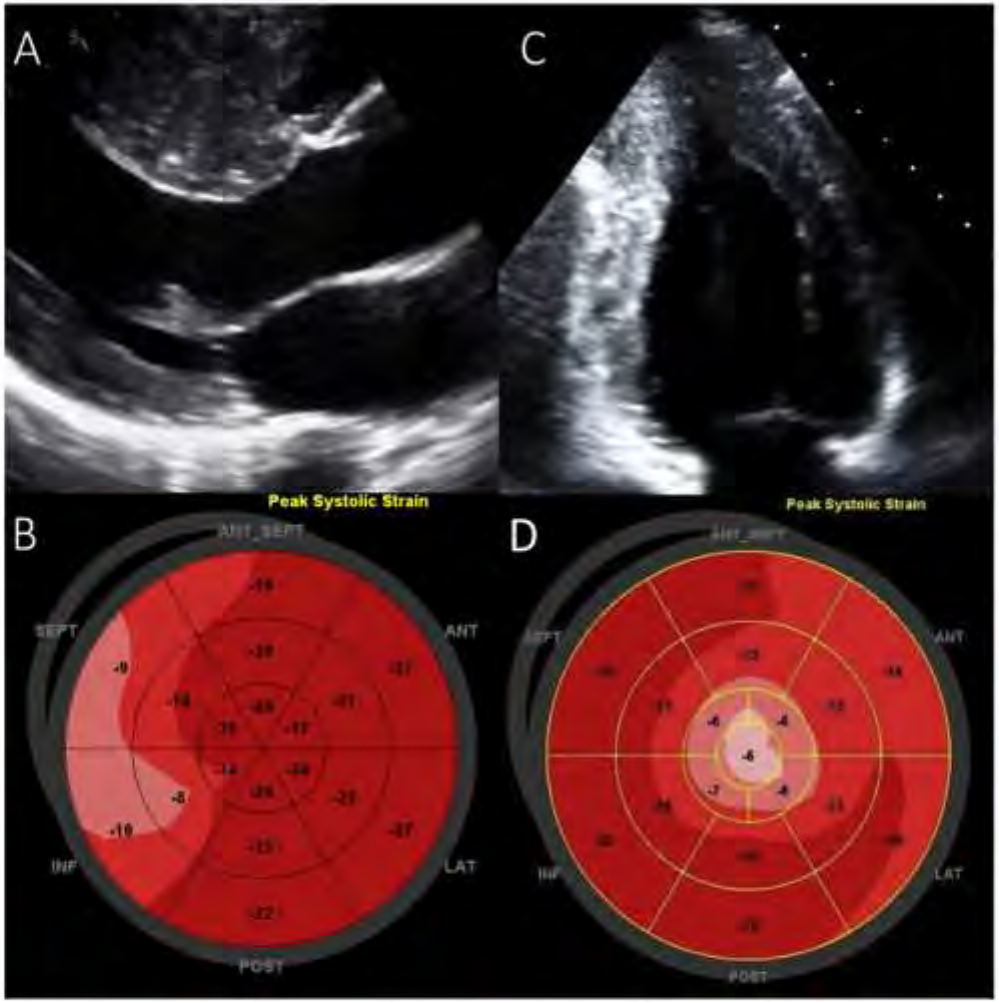


Figure 5 Typical patterns of regional strain in hypertrophic cardiomyopathy (HCM). Parasternal long-axis view of a patient with septal HCM **(A)** with corresponding longitudinal strain polar map **(B)** showing reduction in strain at the septum. **(C)**: An apical 2-chamber view of a patient with apical HCM with corresponding longitudinal strain polar map **(D)** showing reduction in strain at the apex.

Evaluating HCM vs phenocopies

Athlete's heart

- Social history is critically importance regarding type and volume of physical activity.
    - Correlated with 12 lead ECG
        - Look for T wave inversions beyond V4, ST depression, or septal Q waves.
        - 5-10% patients with phenotypic HCM will have normal ECG
- There are difference wall thickness cut-offs depending on race. Black athletes will have wall thicknesses up to 15 that may be considered normal.
        - Most Caucasian athletes, should not exceed 12mm. Generally, there is <1-2mm difference in 2 contiguous segments.

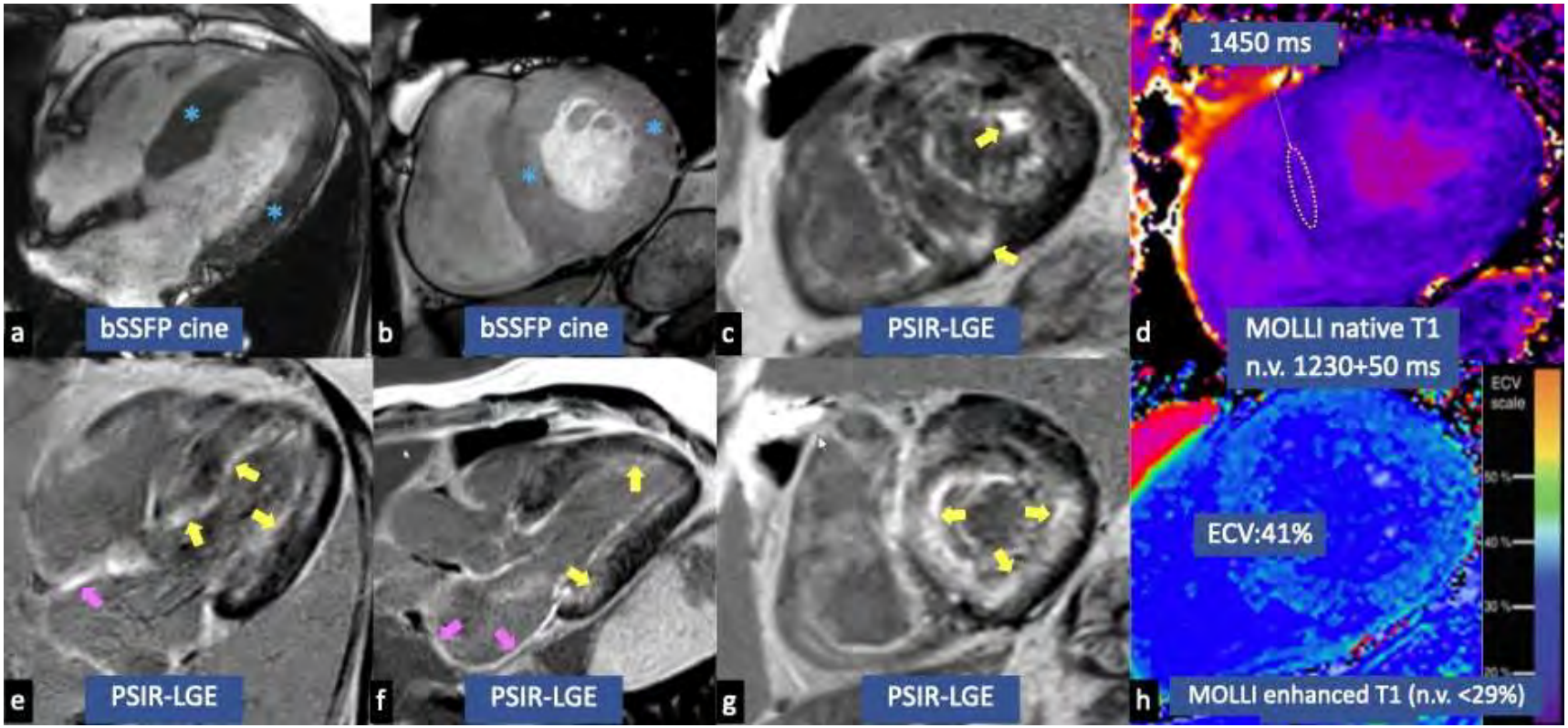
Cardiac Amyloid

- LV wall thickness, biatrial enlargement, marked diastolic dysfunction

- Wall thicknesses can be similar, mean septal and PW thickness was 17 in ATTR. Lower cutoff point for AL amyloid.

- Utilize strain. Classically, would look for apical sparing with "cherry on top". Can reclassify up to 22% of patients.

    - CMR to look for abnormalities in gadolinium pattern, kinetics and expansion of extracellular volume.


a
bSSFP cine
b
bSSFP cine
c
PSIR-LGE
d
1450 ms
MOLLI native T1
n.v. 1230+50 ms
ECV scale
ECV:41%
e
PSIR-LGE
f
PSIR-LGE
g
PSIR-LGE
h
MOLLI enhanced T1 (n.v. <29%)

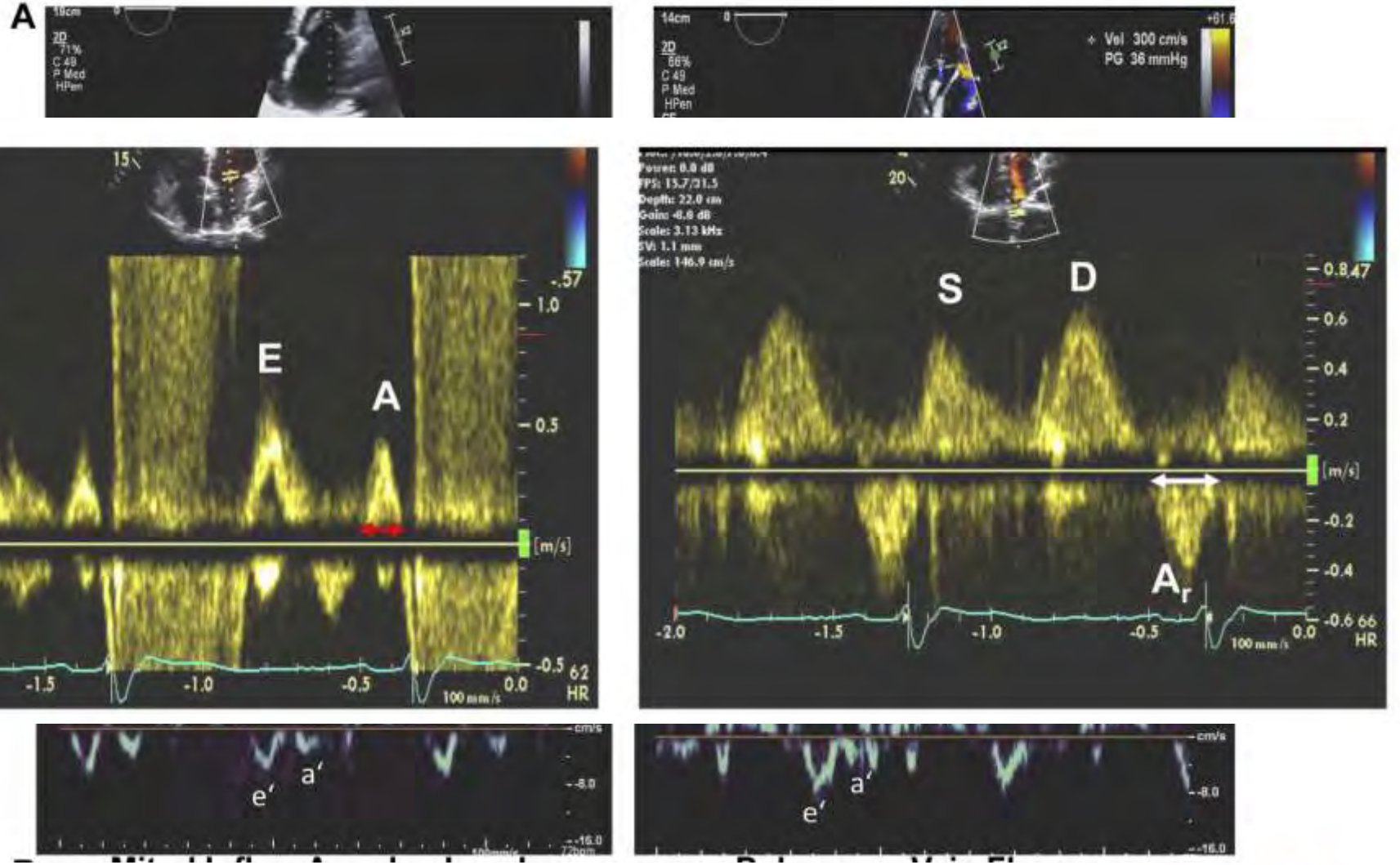
DDx

- Hypertensive heart disease- May be asymptomatic, ECG with LVH and repolarization abnormalities, LVH is usually concentric.
- Anderson-Fabry disease- Mutation in the*GLA* gene. This gene encodes the enzyme α-galactosidase. Presents as a peripheral neuropathy, renal insufficiency. Characteristic decrease in T1 times CMR.
- Danon- Children and adolescents, X-linked dominant, LAMP2 gene mutation
- PRKAG2-Abnormal accumulation of glycogen in myocytes. Presents as myopathy, myalgia, epilepsy, hypertension.
- Fredrichs Ataxia- Loss of DTRs, weakness, dysarthria, diabetes.

Systolic function

- EF should be normal or hyperdynamic in most patients without significant LGE.
- LVEF of <50% is considered abnormal in HCM and is one indication for consideration of ICD.
- UEA improves LV systolic function assessment and concordance with MRI
  - Particularly important for the assessment of apical aneurysm, thrombi, etc.

Diastolic dysfunction



LVOTO and MV abnormalities

- Resting gradient in about 1/3 of patients
  - Thought to be significant when gradient is >30mmHg.
- Provocable in about 1/3.
  - Valsalva, amyl nitrate inhalation, nitroglycerin, squat to stand, exercise.
- Final 1/3 have neither resting or provoked LVOT gradient and classified as having nonobstructive HCM.

**Resting or provocable gradient of >50mmHg is traditional threshold for SRT for drug refractory symptoms.

**Dynamic and frustrating. Varies related to afterload preload, and contractility.

  - Requires a high index of suspicion.

MV and Papillary abnormalities

Elongated mitral valve leaflets are prevalent in patients with oHCM

- Characteristically coapt at the body of the mitral valve and not the tips.

Papillary anomalies can contribute

- Apical or anterior displacement can lead to chordal-leaflet laxity which in turn contributes to SAM.

Look for bifid paps (70%), pap hypertrophy, anomalous insertion (directly into anterior MV leaflet 13%)

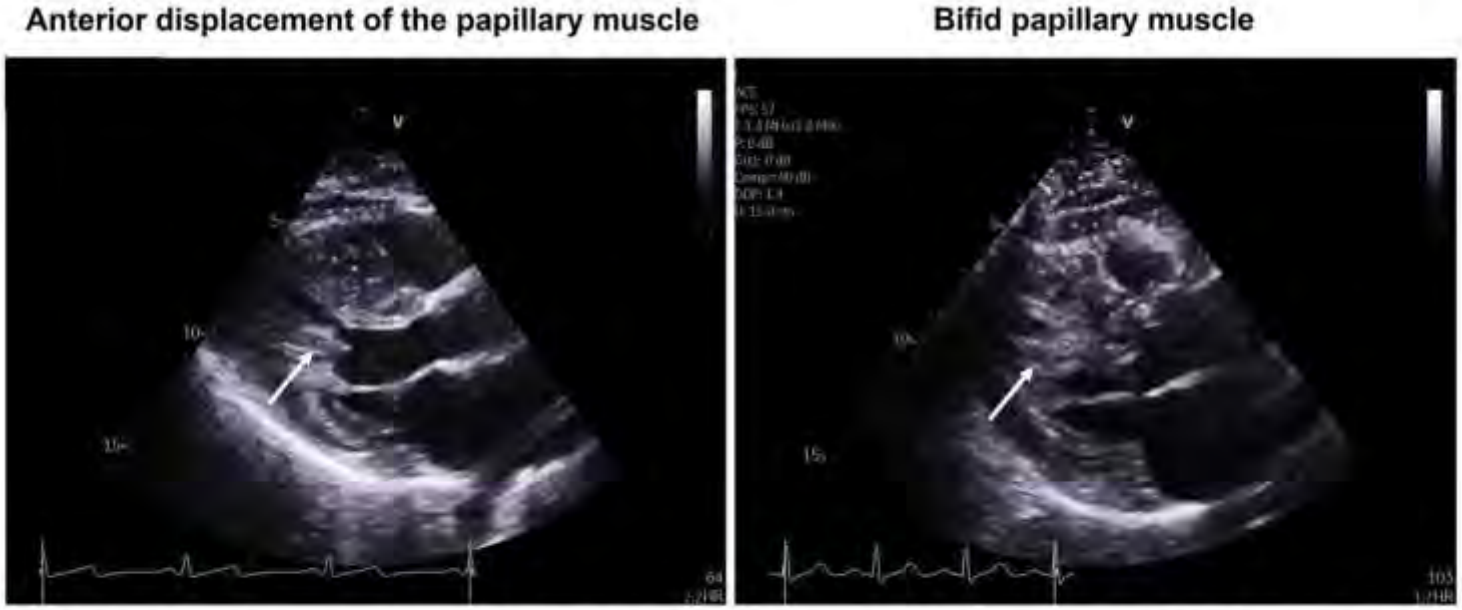


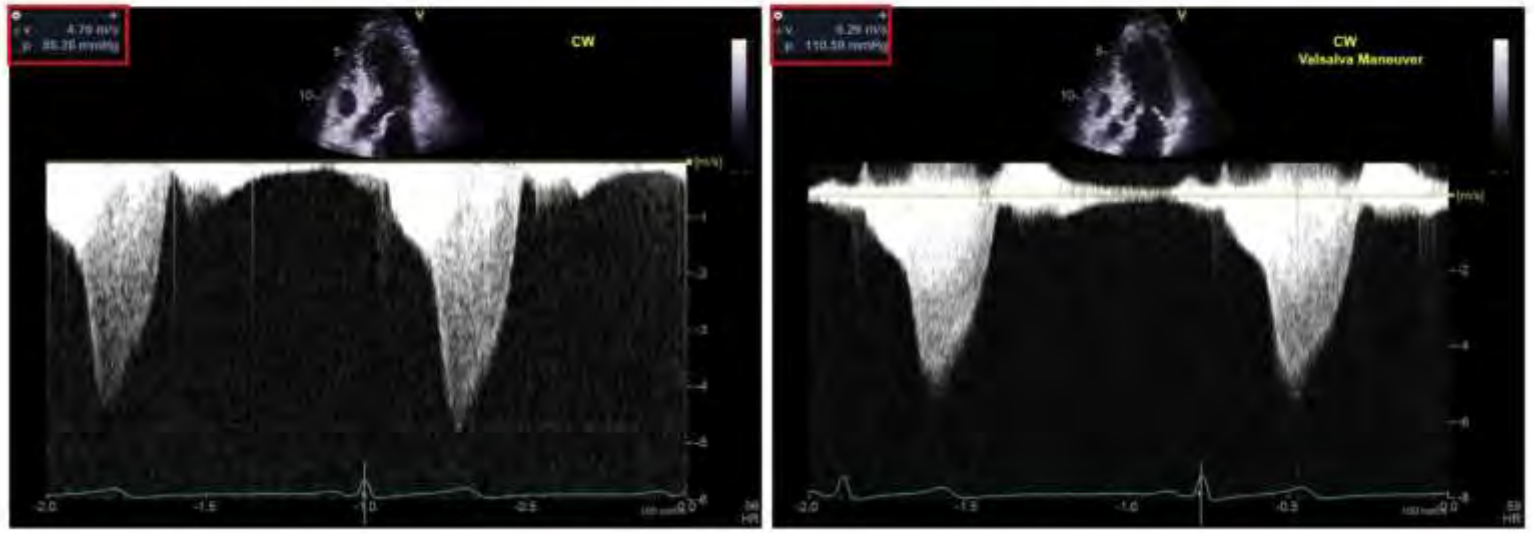
Figure 9 (Left) Parasternal long-axis view (PLAX). Anteriorly displaced hypertrophied papillary muscle (*white arrow*) with a lax chord prolapsing into the left ventricular outflow tract (LVOT). (Right) PLAX. Bifid papillary muscle (*white arrow*) inserting directly to the underbelly of the anterior mitral valve leaflet leading to LVOT obstruction.

Gradient evaluation

CW is the workhorse for determining peak gradient.

- Bernoulli equation correlates well with invasive measures.

Late-peaking, dagger-shaped LVOT velocity waveform at rest and with Valsalva



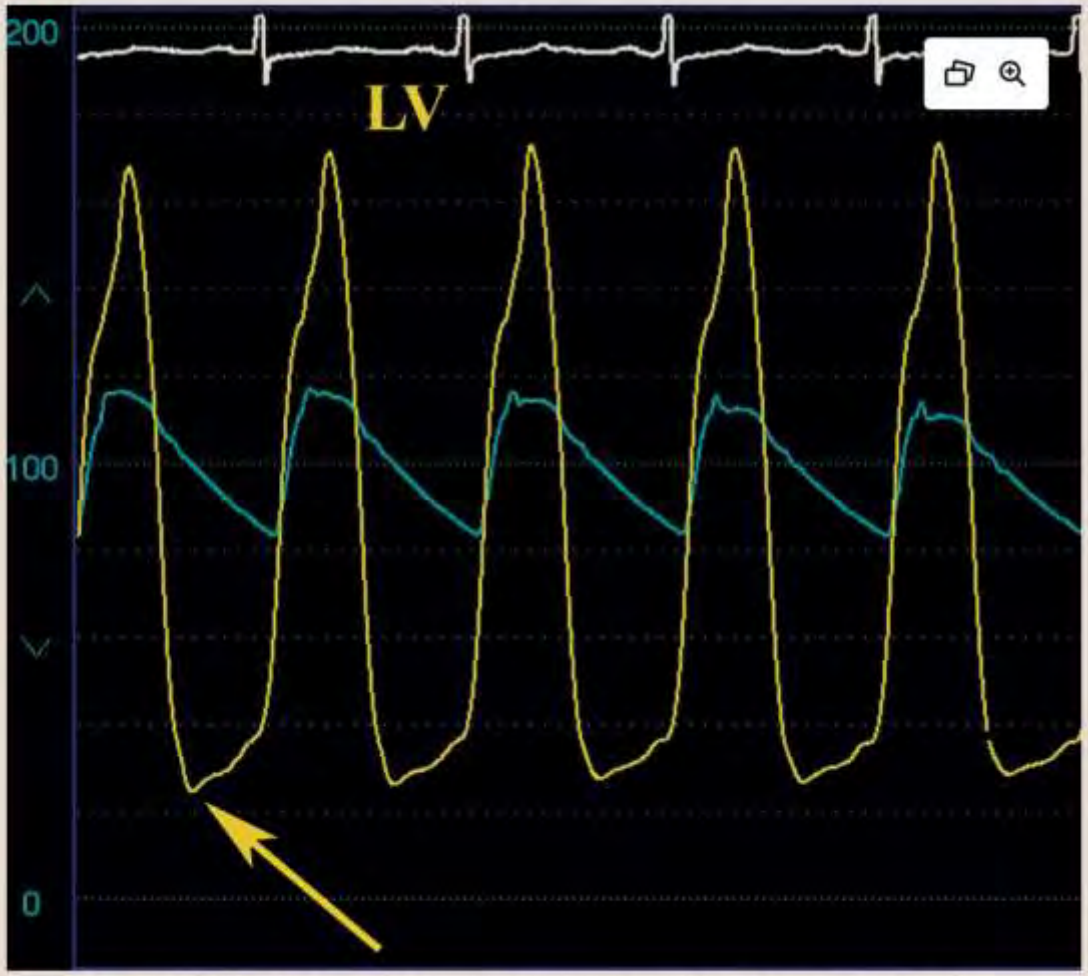
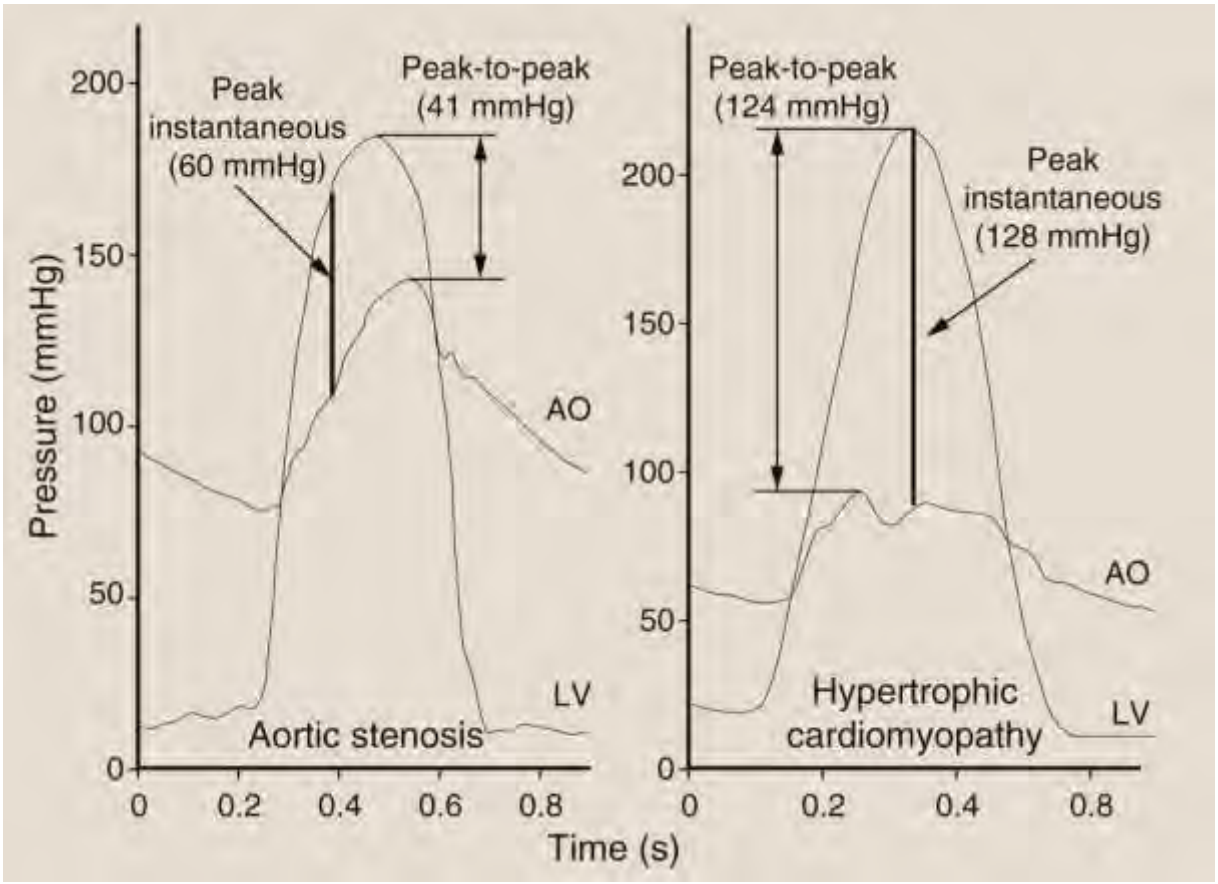


FIG. 6.2 Diastolic dysfunction is common in hypertrophic cardiomyopathy. Abnormal relaxation is manifest by elevation of the early diastolic pressure *(arrow)*, in this case measuring 20 mmHg. *LV,* Left ventricle.


Peak
instantaneous
(60 mmHg)
Peak-to-peak
(41 mmHg)
AO
LV
Aortic stenosis
Peak-to-peak
(124 mmHg)
Peak
instantaneous
(128 mmHg)
AO
LV
Hypertrophic
cardiomyopathy
Pressure (mmHg)
200
150
100
50
0
0
0.2
0.4
0.6
0.8
Time (s)

Methods to provoke obstruction

Postprandial Imaging

Valsalva

- Forced exhalation against closed airway

Squat to stand

- Decrease in preload. Squat for 3 seconds, then stand; repeat x5.

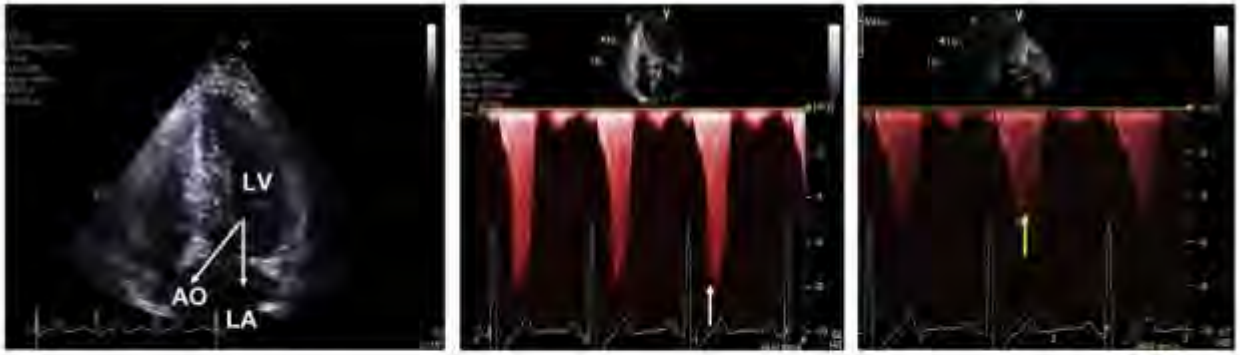
Amyl nitrite

- Potent vasodilator the reduces afterload

Exercise stress echo

- Upright always preferred to supine if able. Supine increases preload and afterload and lower HRR.
- Generally BB and CCB not withheld prior to exercise

Echo math



MR velocity = 7.5 m/s
LA pressure ≈ 20 mmHg
Systolic BP =170 mmHg

LVP - LAP gradient = $4V^2$
4 X $(7.5)^2$m/s = 225 mmHg

LVSP - SBP = LVOT gradient
245 - 170 ≈ 75 mmHg

LVSP = (LV-LA gradient) + LAP
225+ 20 ≈ 245 mmHg

Figure 17 Estimation of the left ventricular outflow tract (LVOT) gradient from mitral regurgitation (MR) velocity using an assumed elevated left atrial (LA) pressure of approximately 20 mm Hg. Applying the modified Bernoulli equation ($4V^2$) to MR velocity of 7.5 m/s (*white arrow*), the gradient between left ventricle (LV) and LA is calculated to be 225 mm Hg. Adding assumed LA pressure to the LV/LA gradient leads to the estimation of LV peak systolic pressure. Once systolic blood pressure is known, in this case 170 mm Hg, it can be subtracted from the LV systolic pressure, yielding the LVOT gradient of approximately 75 mm Hg, corresponding with the LVOT velocity of approximately 4.3 m/s (*yellow arrow*).

FIGU

CENTRAL ILLUSTRATION **Flow Diagram Summarizing Applications of Exercise Testing to Diagnosis and Management of HCM**

Rowin, E.J. et al. J Am Coll Cardiol Img. 2017;10(11):1374–86.

*Diagram assumes HCM patients are at low risk for sudden death and are not candidates for prophylactic implantable-defibrillators. For those HCM patients at increased risk, a sudden death primary prevention strategy may be appropriate, independent of the heart failure management strategies depicted in this figure; †$\dot{V}o_2$ ≤14 ml/kg/min (or ≤50% predicted for age) is the conventional criterion for heart transplant listing (48), although the overall clinical profile of the patient should also be taken into account when considering listing for heart transplant. BP = blood pressure; HCM = hypertrophic cardiomyopathy; HF = heart failure; LV = left ventricular; NYHA = New York Heart Association; $\dot{V}o_2$ Max = maximum myocardial oxygen consumption.

Don't be confounded by the MR jet

Sometimes it is best to start with what is known

- Encourage sonographers to isolate, record and label MR by sweeping CW jet away from LVOTO first.

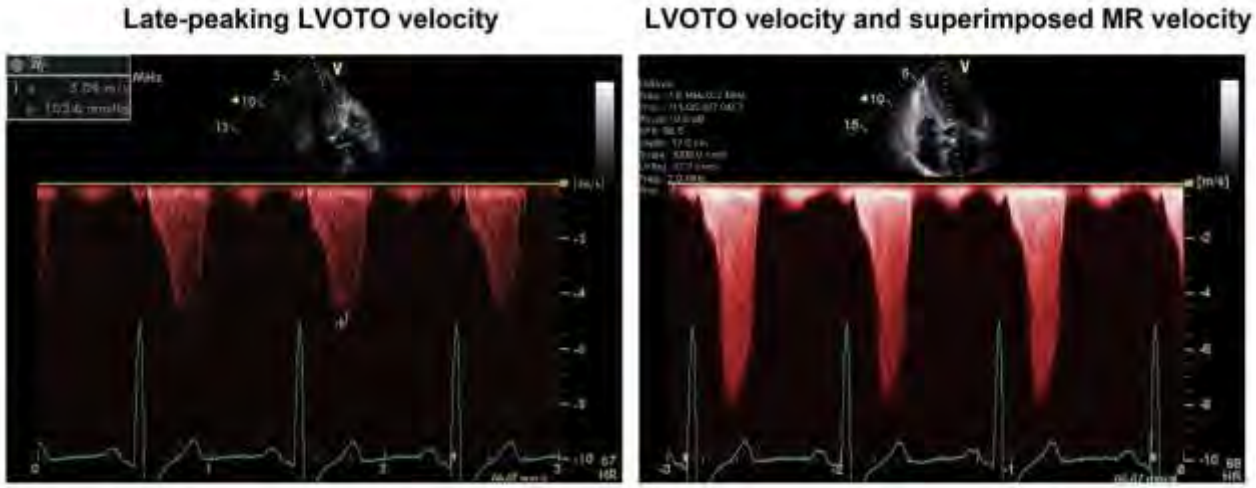
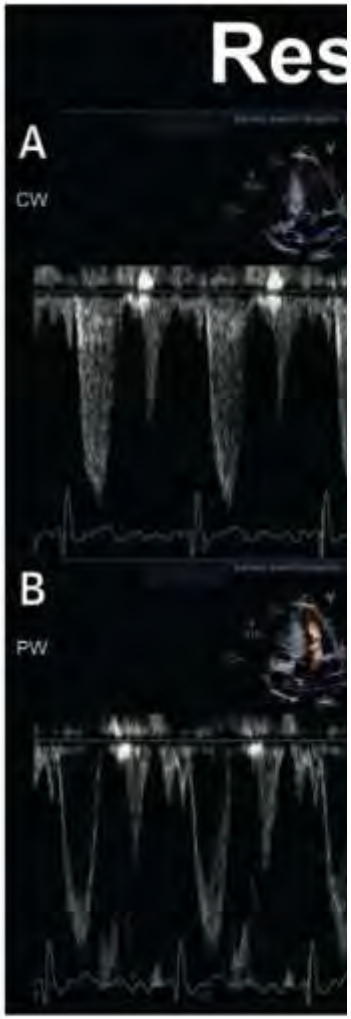


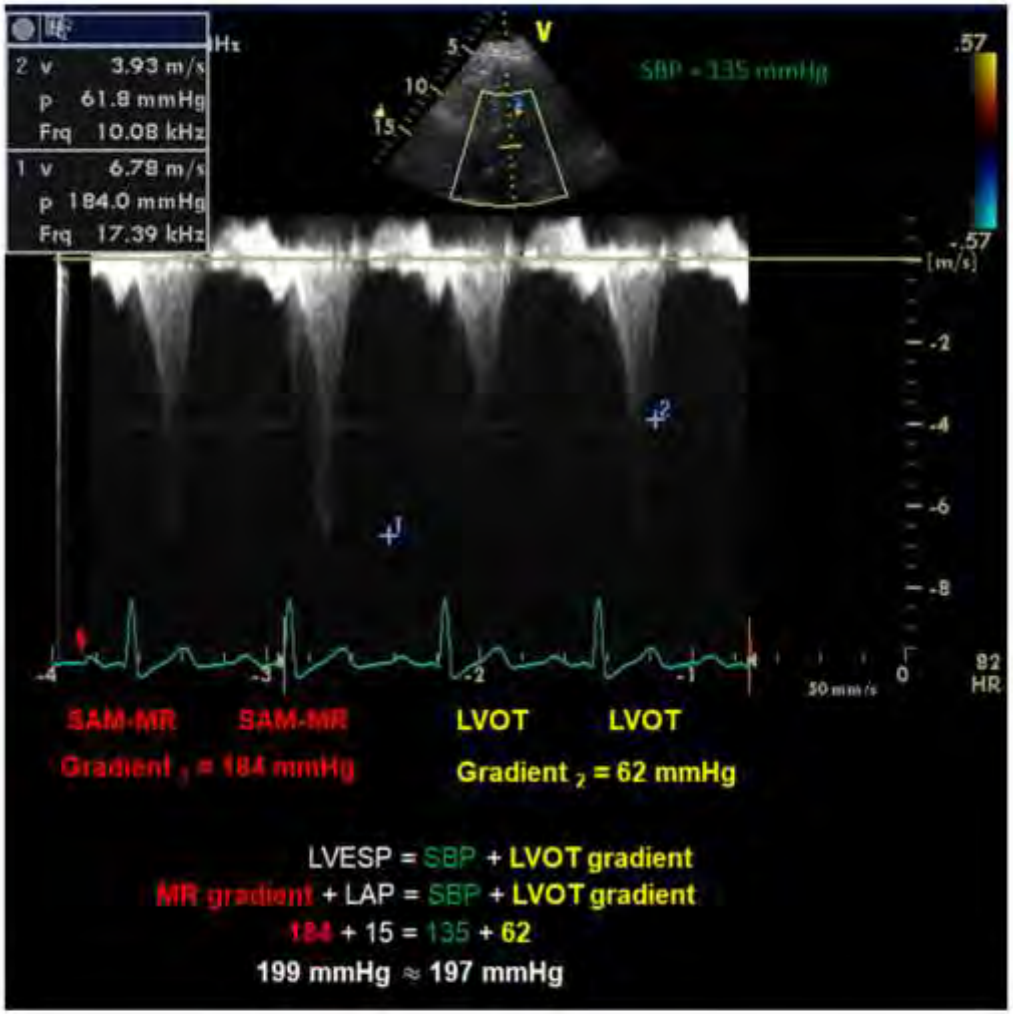
Figure 16 (Left): Apical 3-chamber view. Continuous-wave (CW) Doppler high-velocity late-peaking left ventricular outflow tract (LVOT) flow separated from the mitral regurgitation (MR) flow. (Right): Apical 4-chamber view. CW Doppler waveform containing superimposed velocities: LVOT and MR (peak velocity at 7.5 m/s). When LVOT and MR velocities are superimposed, the highest velocity overestimates the LVOT gradient.

FIGURE 1 Nonobstructive LV



The left ventricular outflow trac
(E, F). Gradients are interrogate

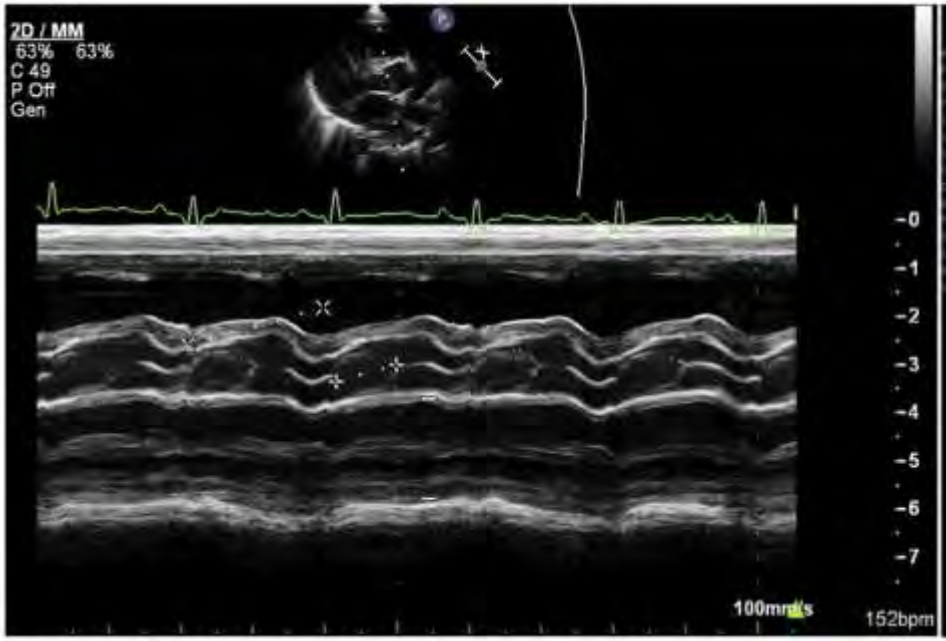
FIGURE 2 Differentiating LVOT Obstruction From SAM-Related MR



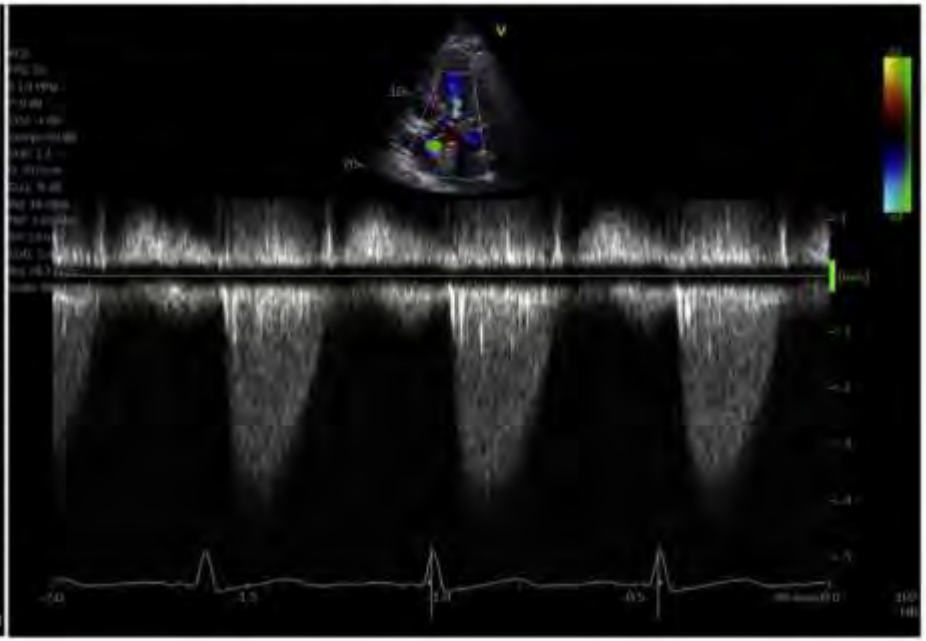
Systolic anterior motion (SAM)-related mitral regurgitation (MR) (first 2 beats) and left ventricular outflow tract (LVOT) velocities (last 2 beats) may both have late-peaking appearances. Using a "back-calculation" from the MR velocity can help confirm the measured LVOT gradient. LVESP = left ventricular end-systolic pressure; SBP = systolic blood pressure.

l after exercise, it is 64 mm Hg
Doppler (D, F).

AV leaflet fluttering



Early-peaking symmetric velocity



have turbulent flow in the LVOT

- Look closely for the absence of SAM, with echo consider the use of "color compare mode".

Coexisting AS

- Must be meticulous in your 2D assessment of the aortic valve.
- Continuity equation is not recommended
  - Planimetry is considered standard
- Simplified Bernoulli equation often cannot be used if proximal velocity exceeding 1.5m/s
  - Modified
- Invasive measures is for when echo fails.

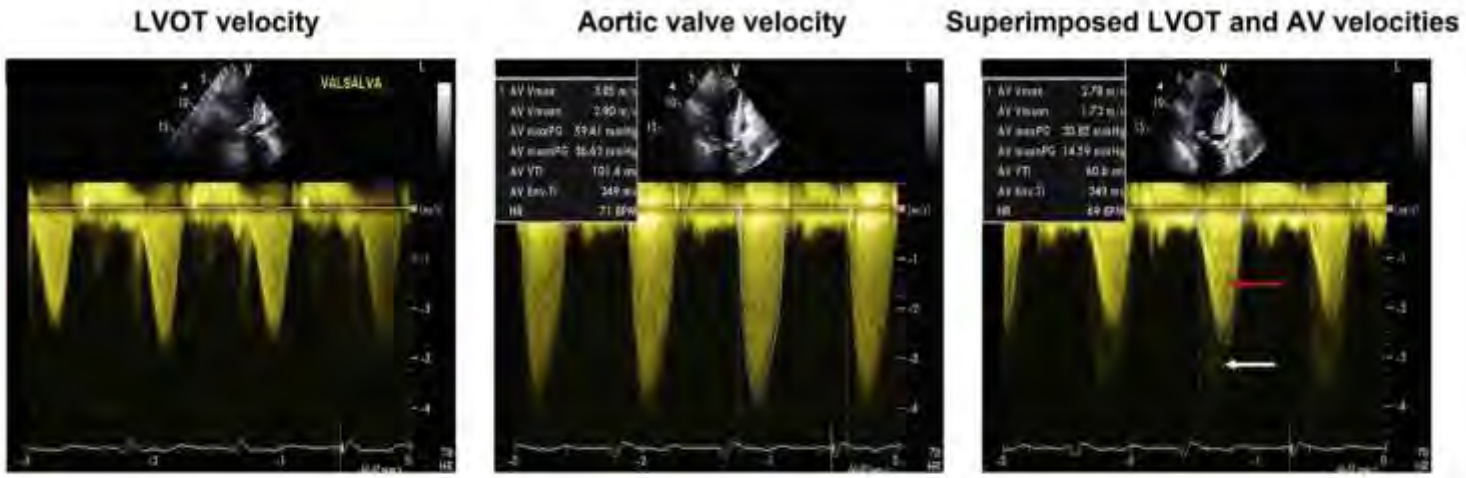


Figure 19 (Left): Apical 3-chamber view. Continuous-wave (CW) Doppler of a mid-to-late peaking left ventricular outflow tract (LVOT) velocity waveform, indicating dynamic obstruction, measuring 2.8 m/s. (Middle): Early-peaking CW Doppler flow velocity that is rounded and reflective of a fixed obstruction, measuring 3.9 m/s. (Right): Superimposed CW Doppler waveforms of LVOT (*red arrow*) and aortic valve (*white arrow*). To estimate approximate transaortic gradient the LVOT gradient has to be subtracted from the aortic valve gradient. In this case the peak gradient calculates to 29 mm Hg and mean gradient is 22 mm Hg.

Pitfalls

SAM is not specific to HCM

Table 2 Differential Diagnosis of SAM and LVOTO
Elderly with hypertension, sigmoid septum and hyperdynamic LV function
Compensatory basal septal hypercontractility following acute myocardial infarction with apical dysfunction
Takotsubo cardiomyopathy with hyperdynamic basal LV function
Massive posterior mitral annulus calcification
After surgical and percutaneous mitral valve repair
After aortic valve replacement in patients with LVH and hyperdynamic LV
Elderly patients in ICU with anemia, volume depletion, tachyarrhythmias, sepsis
Medications eg: inotropes, vasodilators and sympathomimetics
Right ventricular pressure overload like acute COPD exacerbation and/or ARDS
Phenocopies of HCM such as cardiac amyloidosis or Anderson-Fabry disease

Role of CMR

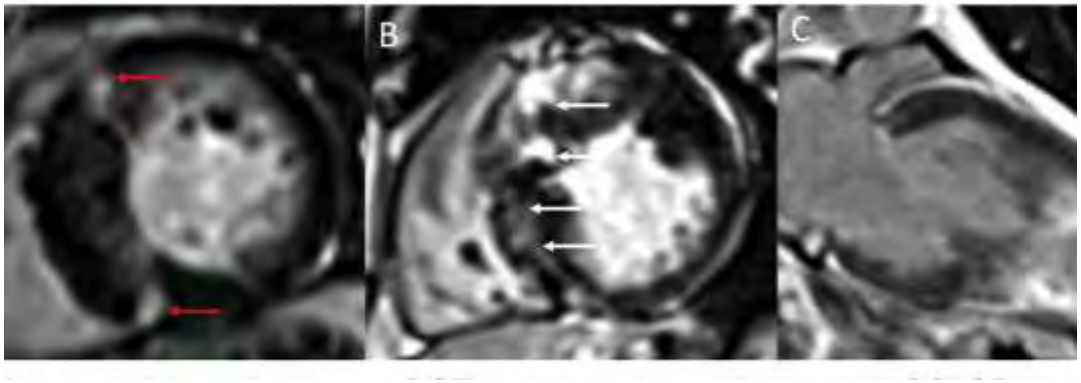
Primary role is adjudicating morphology, best defining function, and tissue characterization with LGE.

Defining wall thickness in any predefined plane.

Exclude phenocopies:

- Amyloid
- HHD
- Fabry's
- Athlete's heart

Can be performed serially every 3-5 yrs to assess for progression in LGE if it would affect clinical decision making.



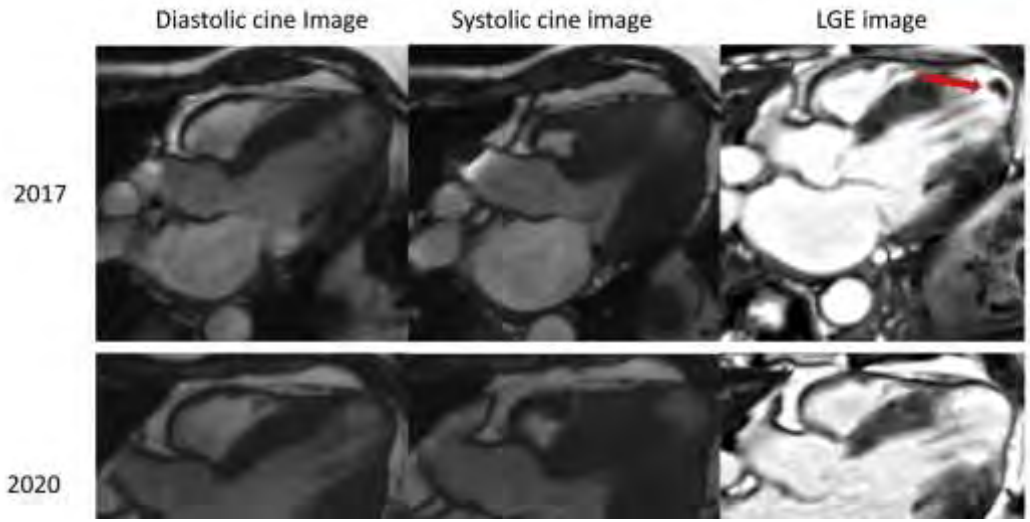


TABLE 8 Clinical Sudden Death Risk Factors for Adults and Children With HCM

Family history of sudden death from HCM	Sudden death judged definitively or likely attributable to HCM in ≥1 first-degree or close relatives who are ≤50 y of age. Close relatives would generally be second-degree relatives; however, multiple SCDs in tertiary relatives should also be considered relevant.[30,31]
Massive LVH	Wall thickness ≥30 mm in any segment within the chamber by echocardiography or CMR imaging; consideration for this morphologic marker is also given to borderline values of ≥28 mm in individual patients at the discretion of the treating cardiologist. For pediatric patients with HCM, an absolute or z-score threshold for wall thickness has not been established; however, a maximal wall thickness that corresponds to a z-score ≥20 (and >10 in conjunction with other risk factors) appears reasonable.[32,33]
Unexplained syncope	≥1 unexplained episodes involving acute transient loss of consciousness, judged by history unlikely to be of neurocardiogenic (vasovagal) etiology, not attributable to LVOTO, and especially when occurring within 6 mo of evaluation (events beyond 5 y in the past do not appear to have relevance).[34]
HCM with LV systolic dysfunction	Systolic dysfunction with EF <50% by echocardiography or CMR imaging.[24,27]
LV apical aneurysm	Apical aneurysm defined as a discrete thin-walled dyskinetic or akinetic segment with transmural scar or LGE of the most distal portion of the LV chamber, independent of size. (In children, apical aneurysm is uncommon, and the risk has not been studied.)[15,16]
Extensive LGE on CMR imaging	Extensive LGE, representing replacement fibrosis, either quantified or estimated by visual inspection, comprising ≥15% of LV mass (extent of LGE conferring risk has not been defined in children).[9-11,20-22,25]
NSVT on ambulatory monitor	≥3 beats at ≥120 bpm has generally been used in studies. It would seem most appropriate to place greater weight on NSVT as a risk marker when runs are frequent (eg, ≥3), longer (eg, ≥10 beats), or faster (eg, ≥200 bpm) occurring usually over 24 to 48 h of monitoring. For pediatric patients, a VT rate that exceeds the baseline sinus rate by >20% is considered significant.[35-37]
Genotype status	Genotype-positive status (ie, harboring a putatively disease-causing pathogenic/likely pathogenic variant) is associated with higher SCD risk in pediatric patients with HCM.[12,14]

bpm indicates beats/min; CMR, cardiovascular magnetic resonance; EF, ejection fraction; HCM, hypertrophic cardiomyopathy; LGE, late gadolinium enhancement; LV, left ventricular; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction; NSVT, nonsustained ventricular tachycardia; SCD, sudden cardiac death; and VT, ventricular tachycardia.

Assessing for ischemia

PET and SPE

- o Due to i general
- o Peak st microva
  - PET dete

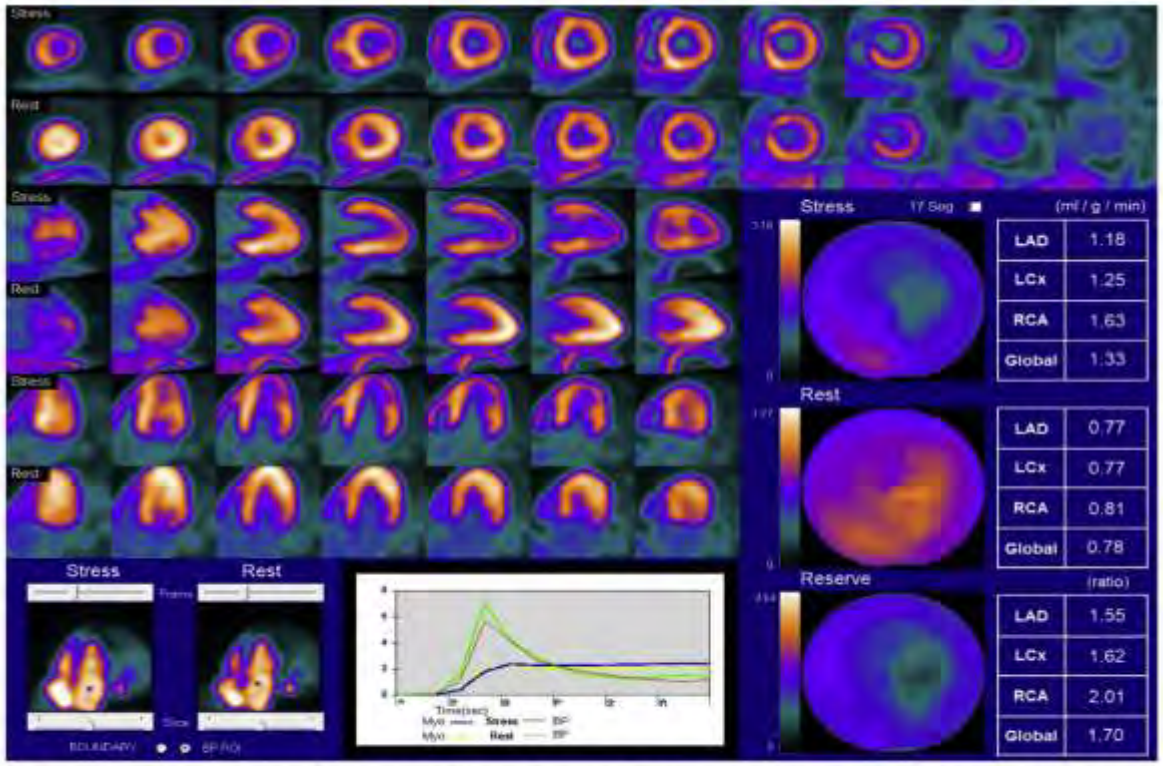
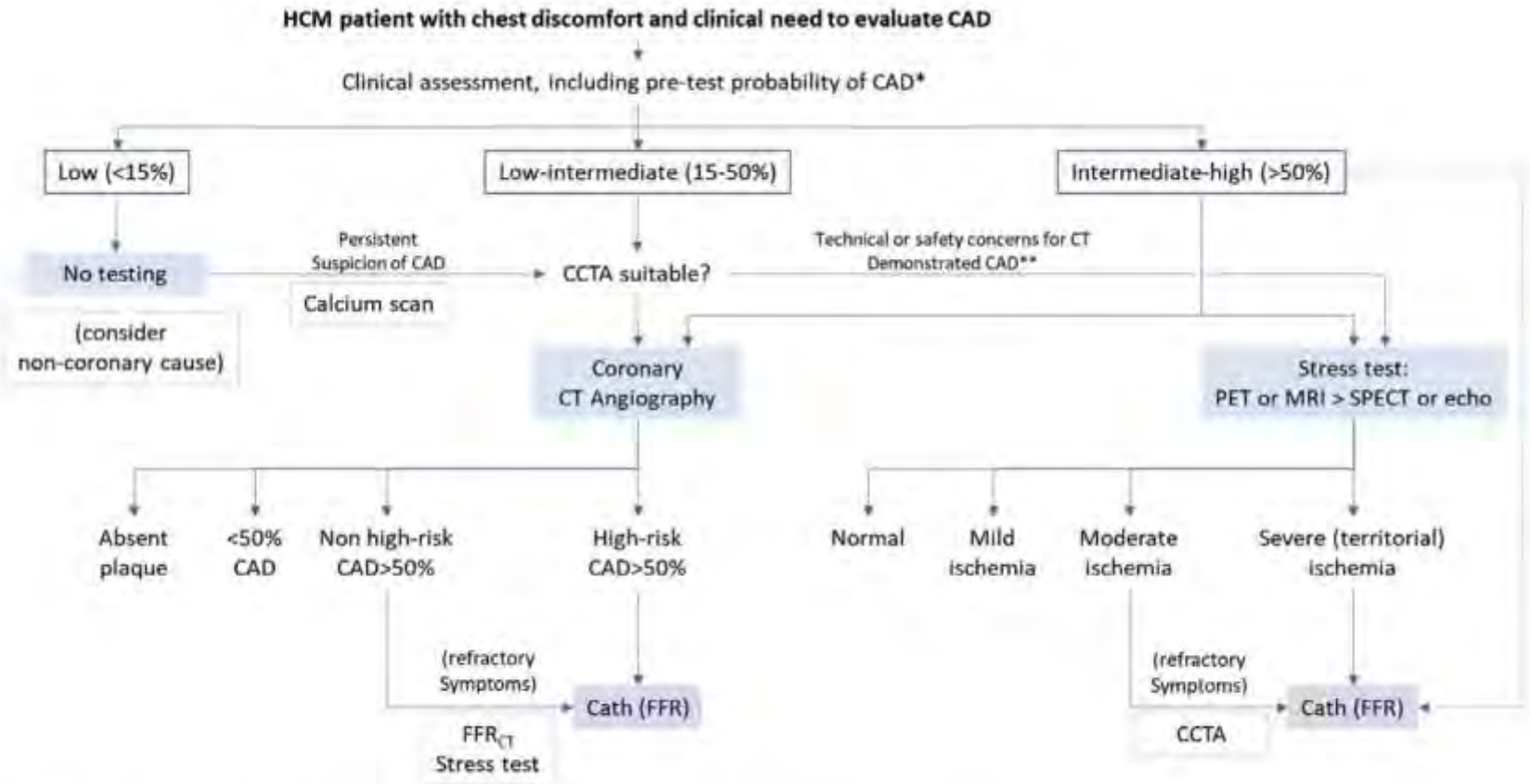


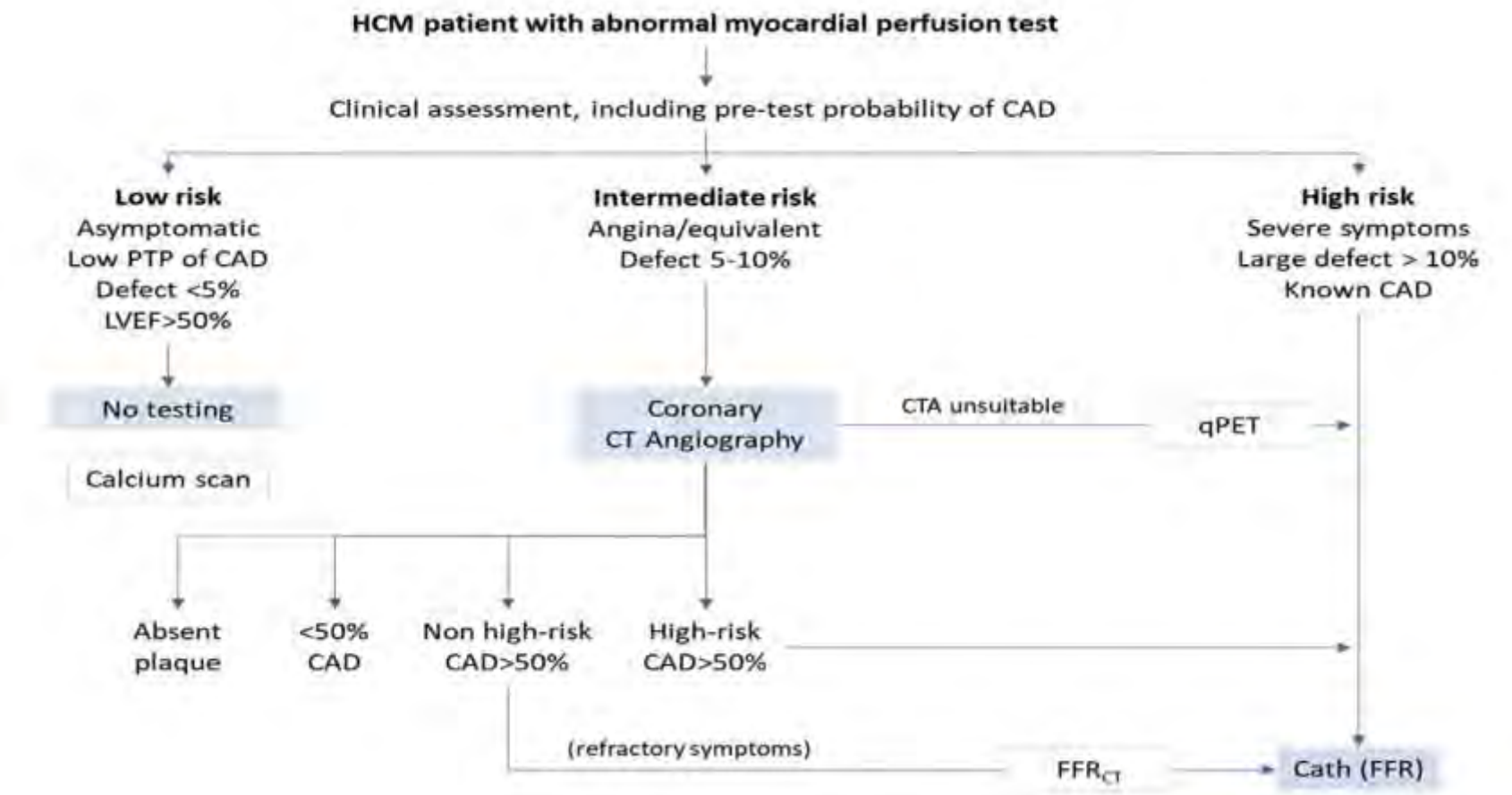
Figure 23 Example of a patient with apical hypertrophic cardiomyopathy. Note the brighter areas of myocardium in the distal lateral wall and apex on the rest images, with decreased perfusion during stress, representing ischemia. There is transient ischemic dilation of the left ventricle with stress, and flow reserve is severely impaired in the distal lateral wall and apex. This pattern often mimics distal left anterior descending coronary artery ischemia.



*Prediction rule

**Safety concerns include pregnancy, contrast allergy, renal impairment; technical limitations include arrhythmia; demonstrated CAD includes CAD>50% by CCTA or ICA, prior infarction, prior revascularization procedures, CCS>1000

What do I do with that?



Cardiac CT

- Useful for
  - For HC
- Same para
  - Low he
  - Reason
  - No sign native v
  - GFR >3
- Nitroglycer with severe
- Generally,
  - Largest

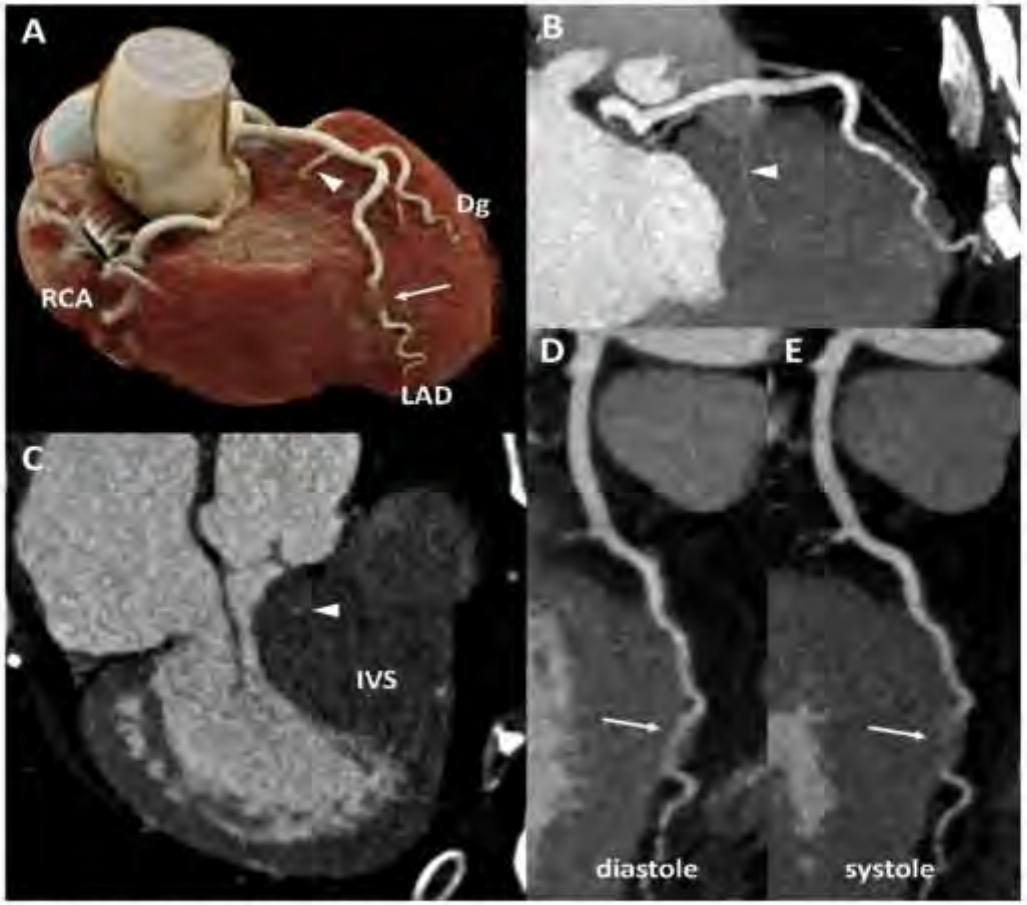


Figure 25 Coronary computed tomography angiogram in a patient with hypertrophic cardiomyopathy demonstrating no atherosclerotic coronary disease. There is myocardial bridging (*arrow*) of the distal left anterior descending coronary artery (LAD) and compression of the vessel during systole (panels **A, D, E**). A large septal branch (*arrow head*) perforates the proximal hypertrophic interventricular septum (IVS) (**A, B, C**). An atrial lead electrode causes limited streak artifacts in the proximity of the right coronary artery (RCA)(A). *Dg*, diagonal branch.

Conclusions

- Imaging is critical in the assessment of patients with known or suspected HCM.

- CMR has a crucial role in the assessment of:
    - LGE, apical aneurysms, papillary abnormalities, indentifying phenocopies.

- Complimentary role of CCTA in coronary assessment

- Imaging guides treatment including medical therapies, SRT, etc.

- Each modality has strengths and limitations. Findings should be discussed with referring team to help further direct their care.

What LV wall thickness (in absence of predisposing condition, or known genetic mutation) is diagnostic of HCM?

a. 12 mm
b. 10 mm
c. 15 mm
d. 14 mm

Which of the following is not a phenocopy of HCM?

a. ARVC
b. Anderson Fabry's disease
c. Cardiac amyloidosis
d. Hypertensive heart disease

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